Validation of the return of spontaneous circulation after cardiac arrest (RACA) score in two different national territories

Luce Caputo, Maria ; Baldi, Enrico ; Savastano, Simone ; Burkart, Roman ; Benvenuti, Claudio ; Klersy, Catherine ; Cianella, Roberto ; Anselmi, Luciano ; Moccetti, Tiziano ; Mauri, Romano ; De Ferrari, Gaetano M ; Auricchio, Angelo

Abstract: BACKGROUND The likelihood of return of spontaneous circulation (ROSC) after out-of-hospital cardiac arrest (OHCA) is influenced by unmodifiable (gender, aetiology, location, the presence of witnesses and initial rhythm) and modifiable factors (bystander CPR and the time to EMS arrival). All of these have been included in the ROSC After Cardiac Arrest (RACA) score. PURPOSE To test the ability of the RACA score to predict the probability of ROSC in two different regions with different local resuscitation networks: the Swiss Canton Ticino and the Italian Province of Pavia. METHODS AND RESULTS All OHCAs occurred between January 1 2015 and December 31 2017 were included. The original regression coefficients for all RACA score variables were applied. The probability to obtain the ROSC as measured with the RACA score was divided in tertiles. Overall, 2041 OHCAs were included in the analysis. The RACA score showed good discrimination for ROSC (AUC 0.76) and calibration, without interaction (p 0.28) between the region and the probability of ROSC. The probability of ROSC was 15% for RACA scores <0.28, 20% for RACA scores between 0.28 and 0.42, increasing to 55% for RACA scores > 0.42. CONCLUSIONS The application of the RACA score reliably assess the probability to obtain the ROSC, with equal effectiveness in the two regions, despite different organization of the resuscitation network. Patients with a RACA score >0.42 had more than 50% probability to obtain ROSC.

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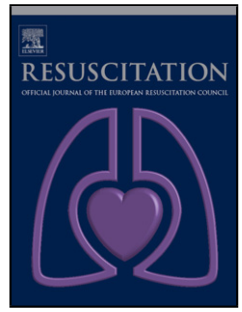

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Validation of the return of spontaneous circulation after cardiac arrest (RACA) score in two different national territories

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ABSTRACT

Background

The likelihood of return of spontaneous circulation (ROSC) after out-of-hospital cardiac arrest (OHCA) is influenced by unmodifiable (gender, aetiology, location, the presence of witnesses and initial rhythm) and modifiable factors (bystander CPR and the time to EMS arrival). All of these have been included in the ROSC After Cardiac Arrest (RACA) score.

Purpose

To test the ability of the RACA score to predict the probability of ROSC in two different regions with different local resuscitation networks: the Swiss Canton Ticino and the Italian Province of Pavia.

Methods and Results

All OHCAs occurred between January 1st 2015 and December 31st 2017 were included. The original regression coefficients for all RACA score variables were applied. The probability to obtain the ROSC as measured with the RACA score was divided in tertiles. Overall, 2041 OHCAs were included in the analysis. The RACA score showed good discrimination for ROSC (AUC 0.76) and calibration, without interaction (p 0.28) between the region and the probability of ROSC. The probability of ROSC was 15% for RACA scores <0.28, 20% for RACA scores between 0.28 and 0.42, increasing to 55% for RACA scores > 0.42.

Conclusions

The application of the RACA score reliably assess the probability to obtain the ROSC, with equal effectiveness in the two regions, despite different organization of the resuscitation network. Patients with a RACA score >0.42 had more than 50% probability to obtain ROSC.

Introduction

The proportion of patients returning to spontaneous circulation (ROSC) after an out-of-hospital cardiac arrest (OHCA) varies considerably in Europe, and even more the 30-day survival (1-3). At the national level, the ROSC rate in patients with attempted cardio-pulmonary resuscitation (CPR) was as high as 50% in Cyprus and as low as 8% in Greece, and survival at discharge from hospital ranging from about 30% in Switzerland and 1% to 2% in Romania (1,4,5). However, comparability of different cohorts has been questioned and direct outcome comparisons may be affected by definitions of inclusion and exclusion criteria and by local resuscitation network organization and performance (6).

In an effort to allow comparison between different EMS systems and patient cohorts, in 2011 Gräsner et al by using data from the German Resuscitation Registry developed, and then internally validated a score to predict occurrence of ROSC after OHCA, the so-called return of spontaneous circulation after cardiac arrest (RACA) (7). The RACA score considers some unmodifiable patient factors such as gender, first rhythm, and OHCA witnessed status as well as modifiable factors including cardio-pulmonary resuscitation (CPR) before EMS arrival, and the time of ambulance arrival. The authors indicated that the RACA score could contribute to preclinical quality assessment, and could help analysing the effects of different resuscitation strategies. The applicability of RACA score to other European EMS systems, first responders network, and population characteristics has been recently performed but somehow conflicting results were noted (4,7). When applied to historical OHCA series recorded in the urban area of the city of Bonn (Germany), RACA score consistently overestimated observed probability of ROSC (4), whereas in study conducted in the city of Helsinki (Finland), a good overall calibration and moderate discrimination of the RACA score was observed (8). Notably, both these study were conducted in physician-staffed urban areas, a resuscitation context different from the one in which the RACA score was developed; thus, unknown is the RACA performance in mixed urban and rural areas. Finally, although RACA score allows a performance comparison of different EMS services in the same country, thus supporting development of strategies to improve outcome, its applicability outside German EMS services is currently unknown.

We hypothesized that RACA score would reasonably predict the probability of ROSC in a territory of two different nations, the Swiss Canton Ticino (a region in the south of Switzerland) and the Italian Province of Pavia (a province in Lombardy, Italy).

METHODS

Study design and setting

This study is a retrospective analysis of all prospectively collected OHCAs occurred between 2015 and 2017 in Swiss Canton Ticino and in Pavia's province. The Ticino Registry of Cardiac Arrest (TIRECA) has been previously described (10). The Pavia Cardiac Arrest Registry (PAVIA CARe) contains the same variables as TIRECA (11); in both registries, data are prospectively collected according to Utstein-style template (12). The study complies with the active guidelines and approved by the scientific committee of the Federazione Cantonale Ticinese Servizi Autoambulanze, and the Fondazione IRCCS Policlinico San Matteo. Furthermore, as a retrospective analysis of clinical routine data this study is in accordance with the country code of medical ethics and was approved by the local ethical competent authority.

Emergency medical system and resuscitation network in Canton Ticino

The Swiss Canton Ticino has a population of 350'363 inhabitants (as of December 31st, 2014); it encompasses a territory of more than 2'800 km² in the southern part of Switzerland. This region presents significant geographic challenges as the territory consists of mountains, valleys, and lakes; the population is distributed among some cities (population ranging from 5'000 to 70'000 inhabitants) and few hundreds of rural municipalities. About 49% of the population consists of men, and overall 21% is over the age of 65 (10). An annual awareness campaign in the education of the resident population in Basic Life Support - Defibrillation (BLS-D) and to set-up a programme for wide availability of a public automatic defibrillator has been promoted by a non-profit organization – Fondazione Ticino Cuore. By December 31st 2017, 16.4% of the resident population had completed a BLS-D course, and there were 797 public automatic external defibrillators (AEDs) in the region.

A national emergency telephone number - 144, is connected to each one of the seven regional EMS dispatching centres operating in Canton Ticino. When a cardiac arrest is suspected, a telephone assisted CPR is initiated until an ambulance arrives. The EMS dispatcher send the ambulance and, in parallel, alerts the traditional first-responders represented by police officers and fire brigade, all trained in BLS-D and equipped with an AED. If the OHCA condition is regarded as safe, the lay responders network is also activated and automatically managed by a mobile application (13). Their training includes the standard Swiss Resuscitation Council Basic Life Support (ERC BLS)/AED course for lay rescuers that complies with the recommendations of the European Resuscitation Council (14).

Each EMS service individually collects data about OHCA interventions in the registry according to Utstein methodology. The data are then reviewed periodically for quality assessment by an internal commission.

EMS and resuscitation network in Pavia's Province

The province of Pavia is a large region (2965 km2) with several rural and few urban areas with a total population of 548.722 inhabitants (as of December 31st, 2014). A national emergency telephone number, 118, is connected to the regional EMS dispatching centre. The local EMS dispatcher coordinates 20 ambulances staffed with BLS-D trained personnel, and 4 ALS-trained staffed ambulances. In case of a suspected OHCA, the EMS dispatcher activates one or two ambulances of which at least with a physician on board and one rescuers' unit, and assists the calling bystander during chest compressions (telephone CPR).

Over the last 10 years, several initiatives have been conducted to improve public education in basic CPR and awareness campaign about the importance to use AEDs even by laypersons (14). By December 31st 2017, 503 PADs were available in Pavia's province (16, 17).

All OHCA data were consecutively and prospectively collected in the PAVIA CARe registry according to Utstein methodology, and periodically reviewed for quality assessment by an internal commission.

Participants

All consecutive OHCAs occurred in adults and collected in both the two registries since 1st of January 2015 until 31st of December of 2017 were considered for inclusion in the study. Patients declared dead before ambulance arrival, with a "do not resuscitate" order or with incomplete data were excluded from further analysis.

Definition of return to spontaneous circulation

As in the original paper by Gräsner et al (7), ROSC was defined as a palpable pulse for ≥ 20 s. Failure of prehospital ROSC with ongoing CPR on admission was considered as a negative outcome (no ROSC).

Statistical analysis

All analyses were performed using Stata 15.1 (StataCorp, College Station, TX, USA). A 2-sided $p<0.05$ was considered statistically significant. Continuous data are reported as mean and standard deviation, median and quartiles when appropriate. Categorical data are reported as counts and percent. Data were compared between groups of patients (by national territory and by ROSC) with the Mann Whitney U test and the Fisher exact test, respectively. The original regression coefficients for all RACA score variables (7) were applied to the combined Ticino and Pavia Registries; the probability of ROSC was calculated from this predictor index and was included as the independent variable of a logistic model for ROSC, to assess discrimination (model area under the ROC curve) and calibration (graphical assessment with the calibration belt (8) of the RACA score in our cohort. Sensitivity and specificity of the model to identify ROSC were also computed. For this purpose patients were classified as ROSC if the predicted probability was equal to or above 0.5. The probability of ROSC was calculated for each patient using the RACA score. Then the distribution of the probability of ROSC was divided in 3 quantiles. Patients' characteristics were compared between tertiles with the Kruskall Wallis test or the Fisher exact test, as appropriate. Then a logistic model for ROSC was fitted with tertiles of the RACA score probability as the independent variables to obtain the corresponding odds ratios (OR) and 95% confidence intervals (95%CI). Model goodness of fit was assessed with the Pearson test and was always satisfied.

Finally we computed the power of showing that the observed area under the ROC curve was above 0.70 (null hypothesis).

RESULTS

During the study period, 3186 had an OHCA and were included in both the two registries. Of these, 1109 patients were declared dead before ambulance arrival or had a "do not resuscitate" order, and 36 patients (1.7%) had incomplete dataset; all these patients were excluded, thus leaving 2041 patients (650 in Canton Ticino and 1391 in Pavia region) for subsequent analysis.

The median age of the patients' population was 74 (IQR 61-82) years old and similar between the 2 regions (Canton Ticino: 71 [65-78] vs. Pavia: 75 [61-82] years, p 0.06). Table 1 summarizes the key demographic characteristics of both the two populations.

Observed ROSC and RACA validation

Overall, a ROSC was obtained in 581 patients (28%) being more frequent in witnessed OHCAs, in those occurred in a public place or at work place, and having a shockable rhythm as first detected rhythm. The overall observed ROSC rate was higher in Canton Ticino than in Pavia region (38% vs. 21%, $p<0.001$) but in both cases lower than the ROSC predicted by RACA score (Ticino: 41% vs Pavia: 31%).

The RACA score model showed a good discrimination (AUC 0.76, 95% CI 0.74-0.78; Figure 1). Observed and predicted ROSC by RACA showed a good calibration ($p=0.65$; Figure 1). Notably, the discrimination capacity in both regions was similar (Figure 2), without significant interaction between the region and the probability of ROSC (test for interaction p 0.28). The power to detect a difference of 0.06 with respect to the null hypothesis was 100%. Overall RACA score reliably predicted the observed ROSC, with a specificity of 90% and a sensitivity of 39%.

The tertiles of probability to obtain the ROSC are reported in Figure 3. The likelihood to observe a ROSC was 15% for RACA score values <0.28, increasing to 20% for RACA scores between 0.28 and 0.42 (OR 1.8, 95% CI 1.3-2.5, $P<0.0001$). RACA scores of more than 0.42 showed a median probability of ROSC as high as 55% (OR 8.3, 95%CI 6.3-11-0, $P<0.0001$). Characteristics of patients included in each of the 3 tertiles were reported in table 2.

DISCUSSION

Our study shows a good overall calibration and discrimination of the RACA score when applied to different resuscitation networks or to different EMS services without interaction between the setting of the resuscitation and predictivity of the score. However, we found that the RACA score has a suboptimal calibration at the two extremes, i.e. in patients with the lowest or highest probability of ROSC. Although these results are encouraging for the applicability of the score in other European countries, it also suggest the need of an adjustment in resuscitation reality dealing with particularly aged population or when there is an overproportion of non-shockable rhythms as we observed.

The original purpose of RACA score intended to be a simple and generally applicable tool for predicting the initial resuscitation success adjusted to clinical conditions and information available to the EMS team on arrival at scene (7). In line with previous experiences (9,18), our study confirms that RACA can reliably predict ROSC in other European countries but significantly expands previous knowledge because the external validation we did was conducted in a mixed reality of both rural and urban cohorts. Indeed, Schewe et al. (18) compared predicted RACA score to observed OHCA ROSC rates in 2070 patients occurring in the city of Bonn (Germany) whereas Kupari et al. performed an external validation of the RACA score in 681 OHCAs occurred in the metropolitan area of Helsinki, Finland (9).

The AUC reported by Gräsner et al. was 0.71 that is consistent with ours. We also noticed the absence of interaction between the region in which the resuscitation was attempted and the performance of the model. As the original model reflected the individual probability of a patient to obtain a ROSC in the German population, our observation may suggest the application of the model in different countries without adjustment of the coefficients considered in the original model. To similar conclusions arrived Kupari et al. in their work (9); indeed they found a performance of the RACA score in terms of discrimination of 0.73, supporting the generalizability of the score. This is a remarkable achievement especially considering some important difference in the proportion of patients aged ≥80 years and the proportion of first rhythm detected. Notably, the difference in demographic variables between our study cohort and the German Resuscitation Registry Group were similar to what recently reported by Kupari et al. (9).

In the conclusive statement of their study, Gräsner et al. said “In EMS teams operating on a high quality level, the observed ROSC rate may be higher than the predicted ROSC rate; the same should be true for a therapeutic intervention and medical treatment having positive effects. Contrarily, where the observed ROSC rate is reasonably lower than the predicted ROSC rate, further analyses of the EMS structure and process quality may be useful to identify reasons for that low performance” (7). Our study was conducted in 2 well defined EMS infrastructures which managed all OHCA cases in a large territory. In our study the observed ROSC was inferior to the expected ROSC, as predicted by RACA score. This finding is consistent with the recent study by Kupari et al. (9) but significantly differs from the single centre German study by Schewe et al. (18) or from a study comparing 7 different centres in Germany when used as one part of the EMS quality assessment in which RACA score underestimated ROSC rates (19). On the other hand and as in the Finnish experience, we noticed that RACA score is significantly lower than the observed ROSC rates, when these latter are particularly high (9). Indeed, in the 9th and 10th decile of probability of ROSC (values >70% of ROSC), Kupari et al. showed a marked difference with the predicted RACA score. In our experience, in the tertile >0.42 we observed a probability of ROSC of at least 0.50 or higher (9). It should noticed that in the work by Schewe et al. who compared predicted and observed ROSC rates over three 5-year time period, the difference between the predicted RACA score and the observed ROSC rate progressively decreased over time (18). One may postulate that this is due to a change in the clinical characteristics of the OHCA patients but more importantly in the proportion and severity of co-mordibities that are not captured by RACA score nor by other predictive scores using survival at discharge and neurological outcome as clinical endpoint, such as the Cardiac Arrest Hospital Prognosis (CAPH) score (20) or the Simplified Acute Physiology Score (SAPS) (21).

To the best of our knowledge, this is the largest external validation study of the RACA score so far published that includes OHCAs occurring in both urban and rural areas at 2 European national territories. The observation that the RACA can be applied in different countries without model adjustment, potentially extends the application of the score to other European countries without further local validation.

Interestingly, most of the national RACA validation studies have used dataset referring to resuscitations attempts occurring before the year 2011 (9,15,16). Since then, European Resuscitation Council guidelines changed. Thus, we assume that our patient cohorts better represents current cardiac arrest patient cohorts and modern post-resuscitation management of OHCA victims. In any case, should a significant discrepancy between predicted and observed ROSC rates been confirmed by other studies, the RACA-scoring system ought to be fine-tuned in order to better fit the observed ROSC rate.

LIMITATIONS

There are some limitations of our study. All patients with incomplete data about OHCA circumstances were excluded from further analysis, which implies a potential selection bias. However, only the 1.7% of all patients included in both registries had incomplete data, which can be considered negligible. All OHCAs in the two registries were classified according to the Utstein template. Considering that the RACA score equation used different categories for etiology and location respect to the Utstein template, some OHCAs in both the two registries were reclassified, accordingly, before apply the RACA score model. Thus some selection bias due to incorrect presumed aetiology or location cannot be ruled out. A potential overestimation of the ROSC probability may be determined by the inclusion of those patients with severe comorbidities, in who the resuscitation was precociously interrupted. However, these patients represent a small subgroup in this analysis, and were not excluded in the original RACA score validation. As in the original RACA score validation, the obtainment of a ROSC was defined by the presence of a palpable pulse for ≥ 20 seconds. The adoption of this definition may have determined an overestimation of the ROSC rate, including also patients in who the resuscitation was only temporarily efficacious. Finally, this validation study of the RACA score was done in two European countries. The potential application of the RACA score in non-European countries needs further validation.

CONCLUSIONS

The application of the RACA score in mixed urban and rural areas is feasible to assess the probability to obtain the ROSC, with equal effectiveness in the two regions, despite different organization of the resuscitation network. Patients with a RACA score >0.42 had more than 50% probability to obtain ROSC. Further studies are needed to assess the applicability of the RACA score as diagnostic tool in the decision-making process of the pre-hospital cardiac arrest resuscitation.

Conflicts of interest

None.

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FIGURES LEGEND

Figure 1. Left panel: Receiver Operating Characteristic (ROC) curve of RACA score; the area under the curve of 0.76 corresponds to a good discrimination of the model in the overall population. Right

panel: Calibration curve for the model in the overall population. The bisecting line corresponds to perfect calibration of the model (perfect agreement between observed deaths and predicted deaths. The line is entirely included in the shaded area corresponding to the 80% and 95% confidence intervals for the observed-predicted relationship, denoting that the model is well calibrated (there is neither over nor underestimation of the mortality).

Figure 2. Receiver Operating Characteristic (ROC) curve of RACA score in Canton Ticino (blu line) and in Pavia's Province (red line).

Figure 3. Tertiles of probability of ROSC by RACA score values.

Figure 1.

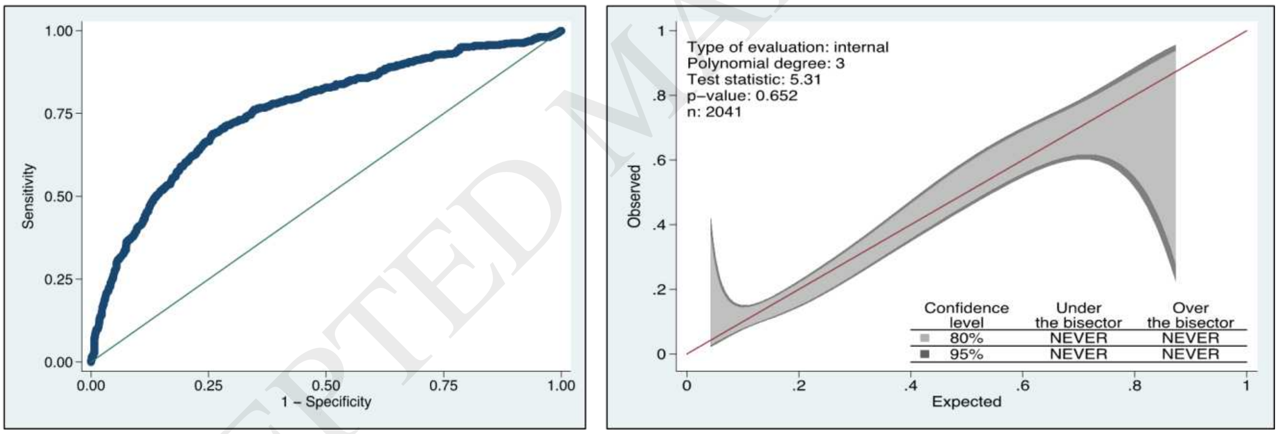


Figure 2.

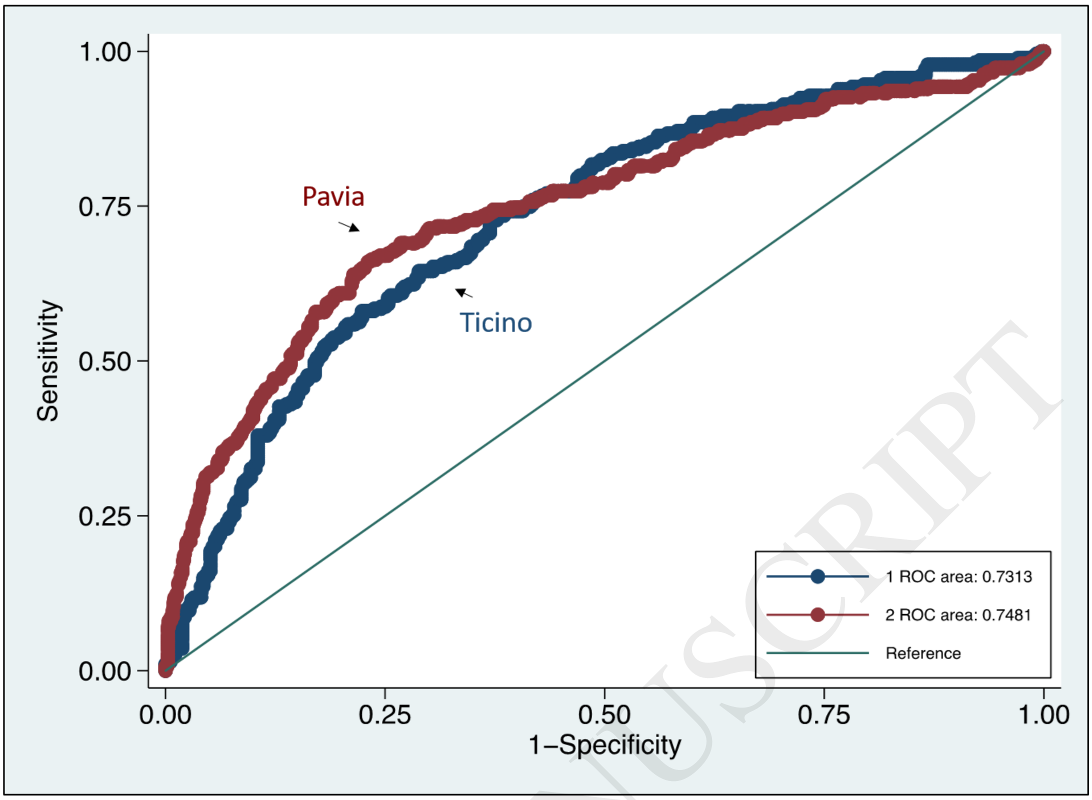
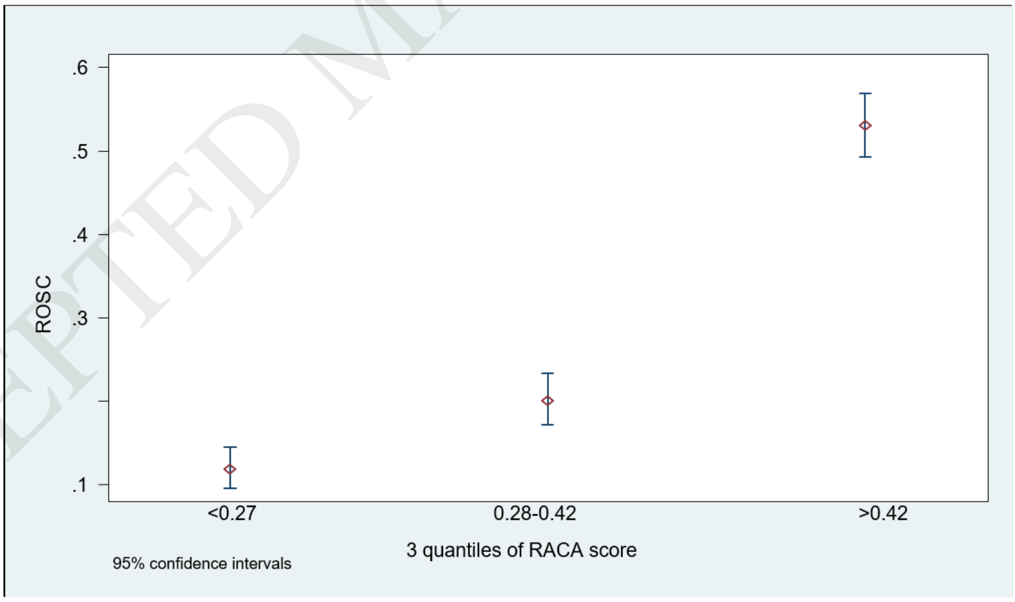


Figure 3.



Tertiles	Odds Ratio	95% CI	P
<0.27	1		
0.28-0.42	1.8	1.3-2.5	<0.001
>0.42	8.3	6.3-11.0	<0.001

Table 1. Demographic characteristics according to RACA score variables.

Variable	All (n=2041)	Ticino (n=650)	Pavia (n=1391)	P value
Male gender, n (%)	1280 (62)	439 (67)	841 (60)	0.005
Age, median (IQR)	74 (61-82)	71 (65- 78)	75 (61-82)	0.06
Age>80 years old, n (%)	808 (39)	205 (31)	603 (43)	<0.001
Etiology, n (%)				0.001
Cardiac	1780 (86)	488 (75)	1292 (91)	
Trauma	85 (4)	23 (3)	62 (5)	
Respiratory	97 (5)	69 (10)	28 (2)	
Intoxication	51 (3)	45 (7)	6 (1)	
Other/unknown	35 (2)	32 (5)	3 (1)	
Witness, n (%)				0.010
None	573 (27)	206 (31)	367 (26)	
Lay people	1112 (53)	317 (47)	795 (56)	
Professionals	352 (20)	132 (22)	220 (15)	
Location, n (%)				0.001
At home	1524 (75)	421 (65)	1103 (79)	

BLS: Basic life support; EMS: Emergency medical system; EMS: emergency medical service.

Nursing home	153 (7)	33 (5)	120 (8)	
Work place	26 (1)	11 (2)	15 (1)	
Doctor's office	17 (1)	17 (2)	0 (0)	
Public place	275 (13)	128 (19)	147 (11)	
other	53 (3)	47 (7)	6 (1)	
Rhythm, N (%)				<0.001
Shockable	408 (20)	149 (23)	259 (19)	
Asystole	931 (45)	266 (40)	665 (48)	
Pulseless activity	566 (27)	207 (31)	359 (26)	
other	143 (7)	35 (5)	108 (8)	
Bystander BLS, N (%)	925 (45)	458 (70)	467 (34)	<0.001
Time to EMS arrival, min (IQR)	10.4 (7.9-14.0)	10.1 (7.6-13.5)	10.6 (8.0-14.0)	0.05

Table 2. Patients' characteristics according to tertiles of the probability of ROSC derived with the RACA score.

Variable	**Probability of ROSC <0.27 N= 689**	**Probability of ROSC 0.27-0.42 N= 677**	**Probability of ROSC >0.42 N=682**
Male gender, n (%)	429 (62)	402 (60)	449 (66)
Age>80 years old, n (%)	353 (51)	289 (43)	166 (24)

Etiology, n (%)			
Cardiac	629 (91)	611 (90)	540 (79)
Trauma	57 (8)	23 (3)	5 (1)
Respiratory	0 (0)	16 (2)	81 (12)
Intoxication	0 (0)	7 (2)	44 (6)
Other/unknown	3 (1)	20 (3)	12 (2)
Witness, n (%)			
None	337 (49)	163 (24)	74 (11)
Lay people	204 (30)	414 (61)	497 (73)
Professionals	145 (21)	99 (15)	111 (16)
Location, n (%)			
At home	561 (81)	549 (81)	414 (61)
Nursing home	68 (10)	51 (7)	34 (5)
Work place	6 (1)	6 (2)	14 (2)
Doctor's office	0 (0)	0 (0)	17 (2)
Public place	53 (7)	62 (9)	160 (24)
other	1 (1)	9 (1)	43 (6)
Rhythm, N (%)			
Shockable	4 (1)	67 (16)	337 (83)

Asystole	508 (73)	333 (49)	90 (13)
Pulseless activity	172 (25)	237 (35)	157 (23)
other	5 (3)	40 (28)	98 (68)
Bystander BLS, N (%)	124 (18)	327 (48)	474 (69)
Time to EMS arrival, min (IQR)	12.0 (9.0-15.0)	10.2 (7.8-13.6)	9.3 (7.0-12.4)
Survival at discharge, N (%)	10 (2)	57 (8)	183 (27)

BLS: Basic life support; EMS: Emergency medical system; EMS: emergency medical service.